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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,039	10/25/2001	Michael A. Adams	PTQ-0039	7209

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EXAMINER

PAK, JOHN D

ART UNIT PAPER NUMBER

1616

DATE MAILED: 06/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/042,039	Applicant(s) ADAMS ET AL.	
	Examiner JOHN PAK	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 1-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 36-40 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/03, 2/05</u> . | 6) <input type="checkbox"/> Other: ____ |

HC

Claims 1-40 are pending in this application.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-10, 15-26, drawn to a method for inhibiting and preventing a malignant cell phenotype, method for increasing efficacy of an antimalignant therapeutic modality against cancer cells, and method of treating cancer in a subject by administering a low dose of a nitric oxide mimetic, classified in multiple subclasses in classes 424 and 514 depending on the chemical structure of the mimetic.
- II. Claims 11-14, drawn to a formulation for inhibiting and preventing a malignant cell phenotype comprising a nitric oxide mimetic, classified in multiple subclasses in classes 424 and 514 depending on the chemical structure of the mimetic.
- III. Claims 27-29, drawn to a prophylactic method for inhibiting and preventing a malignant cell phenotype in animals at high risk for developing cancer comprising administering a low dose of nitric oxide mimetic, classified in multiple subclasses in classes 424 and 514 depending on the chemical structure of the mimetic.
- IV. Claims 30-31, drawn to method of monitoring or diagnosing the progression of a tumor in a patient comprising measuring a level of a tumor marker in a patient in the presence of a low dose of a nitric oxide

mimetic, classified in class 424, subclasses 9.1+, class 435, subclasses 7.1+.

- V. Claims 32-35, drawn to method for decreasing a tumor marker level in a patient comprising administering a low dose of a nitric oxide mimetic, classified in multiple subclasses in classes 424 and 514 depending on the chemical structure of the mimetic.
- VI. Claims 36-40, drawn to "The **use of** a nitric oxide mimetic" for preparation of a medicament for increasing, restoring or maintaining nitric oxide mimetic activity of cells to a level which increases efficacy of an antimalignant therapeutic modality against cancer cells, inhibits and prevents a malignant cell phenotype in an animal, prophylactically inhibits and prevents a malignant cell phenotype in an animal at high risk for developing cancer, or for preparation of a medicament for treating cancer, classified in multiple subclasses in classes 424 and 514 depending on the chemical structure of the mimetic.

The multiple inventions as set forth above are each distinct from the others. The inventions are distinct, each from the other because:

Inventions of Group II and I, III-V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially

different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed can be used in materially different processes as evidenced by the multiple process inventions claimed by applicant (Groups I, III-V), as well as materially different processes for which nitric oxide mimetics are well known for, e.g. treatment of stable angina, prophylactic treatment of phlebitis. The "use of" invention is a separate category of invention, which is not recognized under U.S. patent practice. Distinctness is therefore by default in Group VI.

In addition to the distinctness of the inventions, there would be undue burden placed on the Examiner if the restriction were not required. The list of possible nitric oxide mimetics runs the gamut of chemical diversity. Substances as diverse as nitroglycerin, β -adrenergic receptor agonists, bisphosphonates, superoxide scavenger, adrenergic nerve inhibitor, and adenylyl cyclase activator can be considered nitric oxide mimetics. A complete search of all such substances that fall within the claim scope is a considerable task. Therefore, the search and review of prior art for just one of the invention groups would already be of serious burden for one application. To search and review the prior art vis-à-vis additional distinct inventions, and to make patentability determinations for additional distinct invention groups, would raise the level of search and examination burden in this application to one that would be undue.

Therefore, for the reasons of distinctness and undue burden, the restriction requirement as set forth above is deemed to be proper.

During a telephone conversation with Mr. Snyder on 6/10/2005 a provisional election was made with traverse to prosecute the invention of Group VI, claims 36-40. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

At the outset, the following comments are noted with respect to the "use of" language in claims 36-40. First, said language is not permitted in U.S. patent practice because the "use of" a substance, without more, is not a recognized statutory category of invention. Second, applicant has already provided method claims that recite similar language as the "use of" claims. Therefore, it appears from claim construction that the elected "use of" claims are not directed to processes since separate method claims have already been presented. Prior art-based examination of the elected claims will therefore be confined to a claim interpretation, which limits the "use of" language to its composition embodiment. If in response to this Office action applicant amends the "use of" language to proper method language, then those claims will subsequently be restricted according to the different groups as set forth above in this Office action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one

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or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-40 provide for the use of a nitric oxide mimetic, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 36-40 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 36-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuzmanis (WO 96/30336).

Kuzmanis explicitly discloses a pharmaceutical composition that contains a therapeutically effective amount of a nitric oxide mimetic. See claims 2, 4, 6, and 8. Use in cancer chemotherapy is disclosed. See page 1, the paragraph after the formula; page 3, the paragraph that starts, "For solving mentioned drawbacks" Concentrations of 4.5×10^{-4} M and 4.5×10^{-6} M are explicitly disclosed (page 6, Example 3).

While Kuzmanis does not explicitly state in verbatim language that her pharmaceutical composition "increases efficacy of an antimalignant therapeutic modality against cancer cells," increases, restores or maintains nitric oxide mimetic activity of cells to a level which inhibits and prevents a malignant cell phenotype in an animal or prophylactically inhibits and prevents a malignant cell phenotype in an animal at high risk for developing cancer, Kuzmanis clearly and expressly discloses what is required for anticipation – the use of a nitric oxide mimetic for preparation of a medicament related to cancer treatment. Applicant's "use of" claims can be interpreted so that they

read on a medicament per se. Such medicament is disclosed by Kuzmanis, and the claims are thereby found to be anticipated. MPEP 2112, 2112.01. Specifics of claim 40 are noted, but since the composition and its properties cannot be separated, the cancer treating composition taught by Kuzmanis would have necessarily possessed the properties now claimed by applicant.

Claims 36-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Medline Abstract 96248505.

Medline Abstract 96248505 explicitly discloses low dose arginine, 50 mg/kg of body weight per day, for prophylactic cancer treatment. Survival rate improved, and total number of tumors and total number of malignant and benign tumors were lower in the arginine-treated animal group. Arginine is disclosed to stimulate the immune system at the lymphocyte level and at the macrophage level, induces nitric oxide mediated cytotoxicity against tumor cells.

As discussed previously in this Office action, the claims are interpreted so that they read on a medicament per se. Such medicament is disclosed by the cited reference, and the claims are thereby found to be anticipated. MPEP 2112, 2112.01. Specifics of claim 40 are noted, but since the composition and its properties cannot be separated, the cancer treating composition would have necessarily possessed the properties now claimed by applicant.

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Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JOHN PAK whose telephone number is **(571)272-0620**. The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Gary Kunz, can be reached on **(571)272-0887**.

The fax phone number for the organization where this application or proceeding is assigned is **(571)273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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